

## PATENT COOPERATION TREATY


## PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

REC'D 07 MAR 2005

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| Applicant's or agent's file reference<br>1145WOORD01  | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416) |  |
| International application No.<br>PCT/EP 03/14554  | International filing date (day/month/year)<br>18.12.2003   | Priority date (day/month/year)<br>20.12.2002 |
| International Patent Classification (IPC) or both national classification and IPC<br>A61K31/415   |  |  |
| Applicant<br>ALTANA PHARMA AG   |  |  |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 3 sheets.</p>  |  |  |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> |  |  |
| Date of submission of the demand<br><br>30.06.2004  | Date of completion of this report<br><br>03.03.2005  |  |
| Name and mailing address of the International preliminary examining authority:<br><br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465   | Authorized Officer<br><br>Elliott, A<br><br>Telephone No. +49 89 2399-8218   |  |



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP 03/14554

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-6 as originally filed

**Claims, Numbers**

1-6 received on 27.11.2004 with letter of 25.11.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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EXAMINATION REPORT**

International application No. **PCT/EP 03/14554**

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

|                               |             |     |
|-------------------------------|-------------|-----|
| Novelty (N)                   | Yes: Claims | 1-6 |
|                               | No: Claims  | -   |
| Inventive step (IS)           | Yes: Claims | -   |
|                               | No: Claims  | 1-6 |
| Industrial applicability (IA) | Yes: Claims | 1-8 |
|                               | No: Claims  | -   |

**2. Citations and explanations**

**see separate sheet**

In amended format, the application relates to 8-trialkylsiloxy-2,3-dimethyl-9-phenyl-7-oxo-7,8,9,10-tetrahydro-imidazo[1,2-h][1,7]naphthyridines of formula (1), a process for producing compounds (1a), compounds of formula (3) and the use of compounds of formula (1b) for producing compounds of formula (4).

The following documents will be referred to in this report:

- D1: WO 2003/091253 A (ALTANA PHARMA AG, GERMANY) 6 November 2003
- D2: WO 02/34749 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 2 May 2002
- D3: WO 01/72757 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 4 October 2001
- D4: WO 01/72756 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 4 October 2001 (cited in the application)
- D5: WO 01/72754 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 4 October 2001
- D6: WO 00/17200 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 30 March 2000
- D7: WO 98/42707 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 1 October 1998 (cited in the application)
- D8: WO 01/72748 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 4 October 2001 (cited in the application)

**V Reasoned statement under Art 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

The subject-matter of the present application in amended format is to be regarded as new as the subject-matter of the claims has been restricted (R1 has been restricted to methyl) to overcome novelty objections resulting from the disclosures of documents D2 and D3 in which compounds having R1 being hydrogen are disclosed.

The subject-matter of the present application is however not seen to involve an inventive step as documents D4 and D5 are clearly seen to suggest the subject-matter of the present claims if one considers the reaction scheme on page 22 of D4 and the same on page 26 of D5 and The corresponding accompanying text (G is said to be a hydroxyl group, for example, protected by a suitable silyl radical).

**Other matters:**

1. D1 is not a document to be considered prior art under Rule 64.3 PCT as it was published in the priority interval of the present application. However, depending on the validity of the priorities for D1 and the present application, this document could become relevant upon entry into the regional phases of the present international proceedings. Example II on page 39 contains subject-matter particularly relevant to the subject-matter of the present claims.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

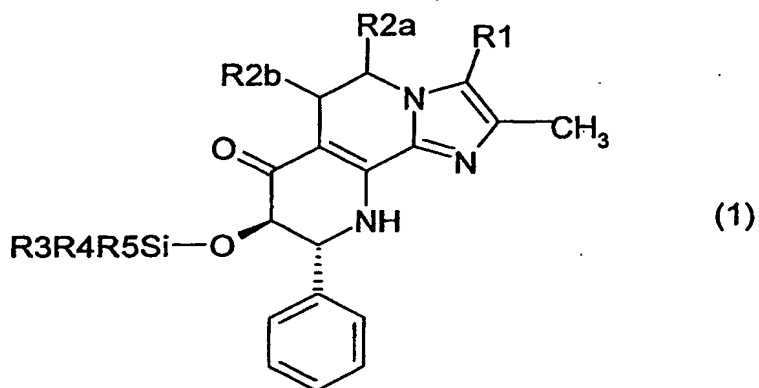
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International application No. PCT/EP 03/14554

2. Contrary to the requirements of Rule 5.1(a)(ii) PCT, neither has the relevant background art disclosed in documents D2, D3, D5 and D6 been mentioned in the description, nor have these documents been identified therein.
3. Due to the amendments to the claims, the description is no longer seen to be in conformity with the claims.

### Claims

1. A compound of the formula 1,



in which

R1 is methyl,

R2a and R2b are both hydrogen or together denote a bond,

R3 is 1-7C-alkyl,

R4 is 1-4C-alkyl and

R5 is 1-4C-alkyl,

and its salts.

2. A compounds of the formula 1 according to claim 1, in which

R1 is methyl,

R2a and R2b are both hydrogen or together denote a bond,

R3 is tert-butyl,

R4 is methyl and

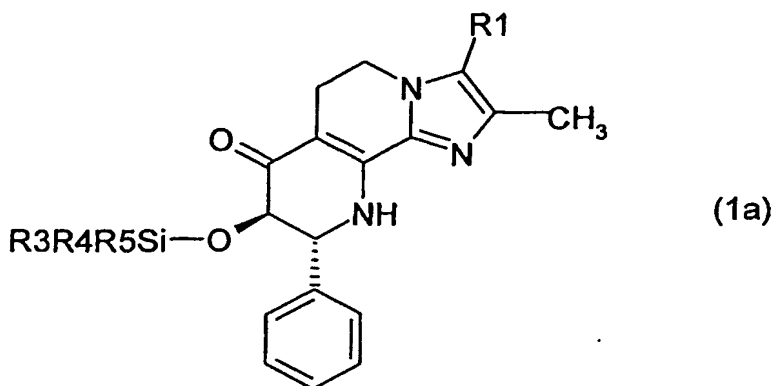
R5 is methyl,

and its salts.

3. A compound of the formula 1 according to claim 1, in which

R2a and R2b are both hydrogen and which is characterized by the formula 1a,

2



in which

R<sub>1</sub> is methyl,

R<sub>3</sub> is 1-7C-alkyl,

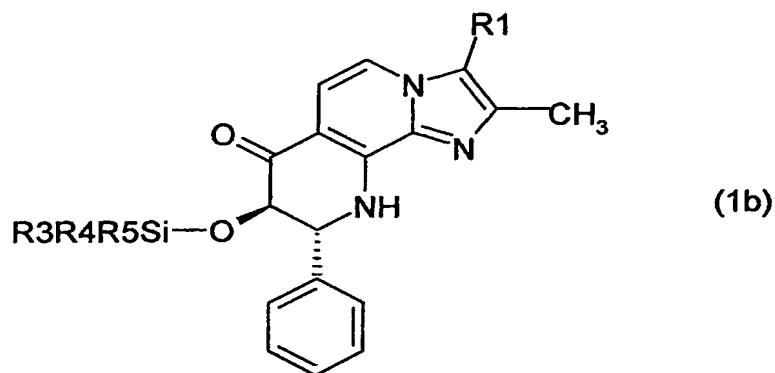
R<sub>4</sub> is 1-7C-alkyl and

R<sub>5</sub> is 1-7C-alkyl,

and its salts.

4. A compound of the formula 1 according to claim 1, in which

R<sub>2a</sub> and R<sub>2b</sub> together denote a bond and which is characterized by the formula 1b,



in which

R<sub>1</sub> is methyl,

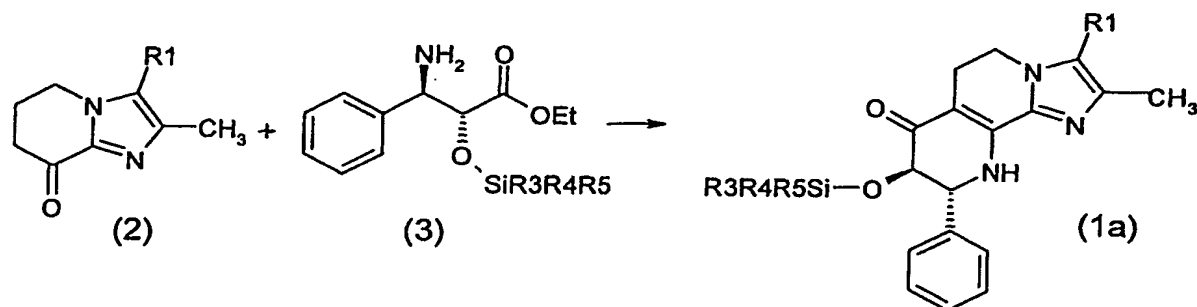
R<sub>3</sub> is 1-7C-alkyl,

R<sub>4</sub> is 1-7C-alkyl and

R<sub>5</sub> is 1-7C-alkyl,

and its salts.

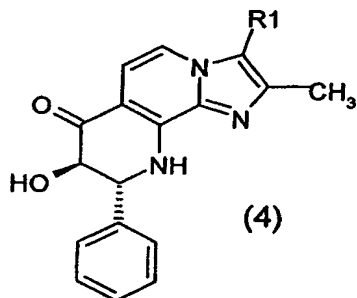
5. A process for the production of a compound of formula 1a according to claim 3,



which comprises reacting a compound of formula 2, in which R1 has the meaning given in claim 3, with a compound of formula 3, in which R3, R4 and R5 have the meanings given in claim 3, and subjecting the resulting imine intermediate to a ring closure reaction.

6. Use of a compound of formula 1b according to claim 4, for the production of a compound of formula

4



in which

R1 is methyl,

by hydrolysis of the compound of formula 1b.